HHS Public Access

Author manuscript

Am J Prev Med. Author manuscript; available in PMC 2018 January 09.

Published in final edited form as:

Am J Prev Med. 2014 September ; 47(3): 233–241. doi:10.1016/j.amepre.2014.05.011.

Comparison of Hepatitis C Virus Testing Strategies:

Birth Cohort Versus Elevated Alanine Aminotransferase Levels

Bryce D. Smith, PhD and **Anthony K. Yartel, MPH**

CDC (Smith) and CDC Foundation (Yartel), Atlanta, Georgia

Abstract

Background—Hepatitis C virus (HCV) infection is unidentified in an estimated 40%–85% of infected adults. Surveillance and modeling data have found significant increases in HCV-associated morbidity and mortality.

Purpose—To compare two HCV antibody (anti-HCV) testing strategies based on (1) elevated alanine aminotransferase levels (ALT) and (2) a birth cohort approach for people born during 1945–1965.

Methods—Data from 19,055 adults aged 20–70 years who completed the National Health and Nutrition Examination Survey in 1999–2008 were analyzed in 2013. Two independent models were evaluated, based on membership in the 1945–1965 birth cohort or elevated ALT, to compare the number of identified anti-HCV-positive (anti-HCV+) individuals; proportion of total identified cases; and the number of people that would be tested using either strategy.

Results—The prevalence of anti-HCV among adults aged 20–70 years was estimated at 2.0% (95% CI=1.8%, 2.3%), representing about 3.6 million people. The birth cohort strategy would result in testing about 85.4 million people and identifying nearly 2.8 million anti-HCV+ people with a sensitivity of 76.6%. The ALT strategy would test about 21.5 million adults and identify approximately 1.8 million anti-HCV+ people with a sensitivity of 50.0%. Implementing both strategies concurrently would identify 87.3% of anti-HCV+ adults.

Conclusions—The birth cohort strategy, which is recommended by both the CDC and the U.S. Preventive Services Task Force, would identify 1 million more anti-HCV+ people than the elevated ALT approach. Concurrent implementation would identify an even larger number of individuals ever infected.

Introduction

An estimated 4 million people have previously been infected with hepatitis C virus (HCV) in the U.S.[1] All individuals infected with HCV develop antibodies (anti-HCV) and about 75%–85% have evidence of HCV-RNA, indicating chronic (current) infection.[1,2] Most people living with HCV infection are adults in their late forties to late sixties and thought to have

Address correspondence to: Bryce D. Smith, PhD, CDC, 1600 Clifton Road, MS: G-37, Atlanta GA 30333. bsmith6@cdc.gov.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

No financial disclosures were reported by the authors of this paper.

been infected 25–45 years ago.[3,4] Without testing and treatment over their lifetimes, the CDC estimates that 60% of people with HCV infection will develop cirrhosis.[5]

In 2007, HCV infection surpassed HIV as an underlying or contributing cause of mortality and accounted for more than 15,000 deaths in the U.S.[6] It is projected that among adults with untreated HCV infection, 37% (1,071,000) will die from complications of hepatitis C in their lifetimes.[5] Recent advances in direct-acting antiviral medications for HCV infection have increased cure rates to 90% in clinical trials.[7,8] However, any benefit from these new treatments requires identification of people with current infection.

Previous studies have estimated that 40%–85% of infected individuals may be undiagnosed and are not aware of their infection, methods to reduce the progression of their liver disease, or behavioral steps to avoid transmission.[9–14] Although risk-based testing can in principle identify approximately 79%–99% of HCV-infected people,[1,15,16] it has been limited in its effectiveness in routine clinical practice.[15,17–21] For example, only 58%–63% of primary care providers inquire about patients' history of risk factors for HCV infection.[19–21] When probed, patients may not fully disclose past or current exposures.[22–26]

Additionally, an estimated 20%–30% of HCV-infected individuals do not report any risk factors and would not be identified by risk-based screening strategies.[13,14,27] It has been suggested that provider motivation and the amount of clinical staff resources (e.g., time) required for adequate and sustainable evaluation of patients for risk factors may represent further limitations to risk-based testing.[13,28,29]

Alanine aminotransferase (ALT) is an enzyme produced by the liver that is a moderately sensitive indicator of liver injury when elevated; therefore, the CDC and the American Association for the Study of Liver Disease both recommend HCV testing for persons with elevated ALT levels.[30,31] Studies suggest that providers are more likely to test patients for HCV based on elevated ALT than on assessment of exposure risk factors.[17,32]

The prevalence of HCV infection among individuals with elevated ALT levels may be several-fold higher compared with those with normal ALT levels.[1,10,11,33] Thus, it has been suggested that HCV testing based on abnormal ALT levels alone could be used to identify 56%–69% of asymptomatic anti-HCV-positive (anti-HCV+) people.[30,34] However, three recent studies[9,15,35] in eight unique primary care settings found that of all people with elevated ALT, 43%–86% were not tested for anti-HCV.

Testing all individuals with elevated ALT would require that these levels be measured as part of routine care and providers have ready access to results; however, current literature[35–38] suggests that only an estimated 46% of patients are evaluated for liver function. The ALT strategy also has other limitations, including lack of a standard definition for the upper limit of normal (ULN)[39,40]; sensitivity to demographic subgroups (i.e., gender, race/ethnicity)[41–46]; alcohol consumption; fatty liver[45]; and the requirement for multiple tests over time to establish persistence.[45,47]

In 2012, the CDC recommended a one-time HCV test[48] for people born during 1945–1965, a high-prevalence cohort that is estimated to account for 67%–76% of adult HCV

infections.[1,16,49] The purpose of this analysis is to compare the sensitivity, number of identified cases, and size of the population that would be tested using either the birth cohort or elevated ALT testing strategy.

Methods

Study Population

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional, nationally representative, multistage, stratified probability cluster survey of the U.S civilian, non-institutionalized population. Each participant is interviewed and medically examined, during which biological specimens are collected for laboratory testing. Information on informed consent procedures, the survey design, and implementation is discussed in the survey documentation.[50] Data collected from 1999 to 2008 were analyzed. Analysis was restricted to participants aged 20–70 years at the time of survey who were interviewed, medically examined, and provided samples for anti-HCV testing. Participants without specimens for testing and those with indeterminate anti-HCV test results were excluded from the final analytic sample.

Outcome Variable

The outcome measure was anti-HCV prevalence as determined by serologic testing. Specimens were tested for HCV antibodies by repeated enzyme-linked immunosorbent assay (ELISA version 3.0; Ortho Diagnostic Systems, Inc., Raritan NJ). All anti-HCV+ specimens were confirmed by recombinant immunoblot assay (RIBA version 3.0; Chiron Corporation, Emeryville CA). Participants who tested positive by both ELISA and RIBA were considered anti-HCV+. Further, HCV-RNA testing results were not available for all cycles of NHANES and were not included in this study.

Anti-HCV Testing Variables

Participants' birth year and ALT levels were selected as the variables for evaluation of anti-HCV testing strategies. Birth year was estimated by subtracting participant age at time of survey from the estimated year in which the participant was surveyed.[51] Persons with birth year 1945–1965 were classified as being within the birth cohort. Elevated ALT was defined as ≥40 IU/L based on a one-time measurement of serum ALT activity (Hitachi 917, Roche Diagnostics, Indianapolis IN [1999–2001]; Beckman Synchron LX20 and DxC800, Beckman Coulter, Inc., Fullerton CA [2002–2008]). The analytic sensitivity and range of the different analyzers were similar and the distributions of ALT activity did not differ significantly.[52–58]

Other Variables

The following demographic and risk factors were included based on review of the literature[1,49] and public health significance: race/ethnicity; gender; veteran status; family income; health insurance status; daily alcohol consumption within the past 12 months; lifetime injection drug use (IDU; cocaine, heroin, and methamphetamine); and history of blood transfusion before 1992. NHANES questions related to history of injection drug use

are restricted to adult participants aged 20–59 years. All analyses involving IDU were similarly restricted.

Statistical Analysis

Weighted means, proportions, SEs, and 95% CIs were estimated to describe participant characteristics. Weighted estimates of anti-HCV prevalence were derived for all adults aged 20–70 years and by subgroups. Differences in prevalence between subgroups were determined by specifying linear contrasts. Statistical significance was defined as a two-sided p-value < 0.05.

Two models were evaluated using the birth cohort and ALT testing strategies applied to the target population of persons aged 20–70 years. For the birth cohort strategy, it was assumed that all persons born during 1945–1965 would receive a one-time anti-HCV test. Sensitivity was defined as the number of anti-HCV+ people within the birth cohort divided by the total number of anti-HCV+ individuals aged 20–70 years.

Similarly, for the ALT strategy, it was assumed that all participants would have ALT test results available and those with elevated ALT levels would be tested for anti-HCV. For this strategy, sensitivity was calculated as the number of anti-HCV+ people with elevated ALT divided by the total number of anti-HCV+ people aged 20–70 years. Sensitivity analyses were subsequently performed to examine the impact of (1) using alternate cut-off levels for the ALT ULN (i.e., 31 U/L for men and 20 U/L for women, in comparison to the standard 40 U/L for both genders)[45] or (2) testing everyone in the 1945–1965 birth cohort in addition to testing adults outside the birth cohort who have elevated (≥40 U/L) ALT levels.

Data were analyzed using SAS-callable SUDAAN, version 10.0.1 (RTI International, Research Triangle Park NC) to account for the complex survey design. Sampling and design variables published by NHANES were used to account for the probability of being medically examined and tested for anti-HCV.[50] Sample weights were rescaled after combining data across multiple survey years.[59] Variance and SEs were estimated using the Taylor linearization method. Data analyses were completed in 2013.

Results

Participant Characteristics

The estimated interview response rate for adults aged 20–70 years from 1999 to 2008 was 76.4% (n=21,313/27,897) (Figure 1). Of the 21,313 participants who were interviewed, 20,341 (95.4%) were medically examined and 19,130 provided specimens for anti-HCV testing. The final analytic sample consisted of 19,055 participants (93.7% of those examined) following exclusion of participants with indeterminate anti-HCV results (n=75).

Characteristics of the study population are reported in Table 1. The average age of the participants was 42.7 years (SE=0.2 years). Approximately 10.9% (95% CI=9.4%, 12.6%) of participants were non-Hispanic black; 46.8% (45.8%, 47.9%) were in the birth cohort; 2.1% (1.8%, 2.5%) reported past or current injection drug use; 6.3% (5.9%, 6.8%) received

blood transfusion before 1992; and 11.8% (11.2%, 12.4%) had elevated ALT levels (Table 1).

Among anti-HCV+ participants, 43.4% (95% CI=37.6%, 49.5%) reported a history of IDU; 15.2% (11.3%, 20.1%) received blood transfusion prior to 1992; 57.6% (51.4%, 63.5%) reported drinking two or more alcoholic beverages per day; and 34.7% (29.2%, 40.5%) were uninsured (Table 1). Cumulatively, people with a documented history of IDU or blood transfusion accounted for 53.8% (48.4%, 59.2%) of anti-HCV+ participants.

Prevalence of Anti-HCV

Anti-HCV prevalence estimates are reported in Table 2. The overall prevalence of anti-HCV among adults aged 20–70 years was estimated at 2.0% (95% CI=1.8%, 2.3%). Based on population estimates from the 1999–2008 Current Population Surveys,[60] this corresponds to about 3.6 million non-institutionalized civilian adults with HCV antibodies. Anti-HCV prevalence was higher among participants born during 1945–1965 (3.2% [2.8%, 3.8%]) compared to those outside the birth cohort (0.9% [0.7%, 1.1%]), as well as among participants with elevated ALT levels (8.4% [7.0%, 9.9%]) compared to those with normal ALT levels (1.1% [0.9%, 1.3%]).

Comparison of Birth Cohort and ALT Testing Strategies

The average population of adults aged 20–70 years represented in the 1999–2008 NHANES cycles was nearly 182.8 million.[60] Using the birth cohort strategy as the testing criterion, about 85.4 million people would be tested for anti-HCV and about 2.8 million individuals with anti-HCV would be identified, yielding a sensitivity of 76.6% (Table 3). In contrast, the ALT strategy would result in testing 21.5 million adults and identifying 1.8 million anti-HCV+ people with a sensitivity of 50.0%. In addition, assuming that 75%–85% of anti-HCV + persons are currently infected, testing everyone within the birth cohort would identify an estimated 2.1–2.4 million current HCV infections compared to 1.4–1.5 million for the ALT strategy (Table 3).

In a sensitivity analysis using a ULN of 31 U/L for men and 20 U/L for women,[45] it was estimated that 72.8 million adults would be tested and 75.7% of anti-HCV+ people (men=75.1%, women=76.8%) would be identified. If the birth cohort strategy was implemented, and, at the same time, the ALT strategy was implemented among people outside the birth cohort, 87.3% of anti-HCV+ adults aged 20–70 years would be identified.

Discussion

Our findings indicate that targeting the high-prevalence birth cohort for HCV testing has the potential to identify about 1 million more anti-HCV+ people compared to a strategy based on a single elevated ALT result. The prevalence of anti-HCV within the birth cohort is about four times that in the adult population born before 1945 or after 1965, and using the birth cohort as the basis of anti-HCV testing would identify nearly 77% of anti-HCV cases in the U.S. adult population compared to 50% identified using the ALT strategy.

Most adults currently living with HCV were likely infected 25–45 years ago[3,4] and may not admit to or recall past behaviors that put them at risk for HCV infection. The high prevalence of HCV infection in the 1945–1965 birth cohort is most often the consequence of receipt of a blood transfusion prior to 1992 or of IDU[1,4]; others may have acquired HCV infection through health care (e.g., kidney dialysis) or use of blood-clotting products.[4,49,61] Although our analysis confirmed IDU and blood transfusion as important transmission risk factors responsible for more than 54% of anti-HCV+ cases, another 46% did not report either of these exposure risk factors. The birth cohort testing strategy does not rely on solicitation of risk factors and would test all members of the birth cohort even if they do not disclose historic exposures to HCV risk factors.

In contrast, the ALT strategy would mean testing 60 million fewer people but would fail to identify approximately 700,000–900,000 with current HCV infection (Table 3). By various estimates, approximately 30%–50% of individuals with current HCV infection demonstrate persistently normal ALT levels (PNALT)[62–65] and would not be identified by an ALT test. More concerning, one third of HCV-infected people with PNALT have significant fibrosis progression and could be treated if diagnosed.[65–66] Other limitations of the ALT strategy include sensitivity to age, race, gender, and alcohol consumption[44–46] and the need for multiple tests over time to establish persistently elevated ALT levels in patients.[44]

These findings are supported by previous studies: A recent study found that a testing strategy based on the 1946–1964 birth cohort would identify 76% of anti-HCV+ people[16]; other studies have produced similar estimates using the 1945–1964 birth cohort.[1,47] Likewise, our finding that the ALT strategy would identify 50% of anti-HCV cases is consistent with previous population-based estimates.[64,65] The birth cohort strategy has been found to be cost-effective[67–69] and adoption of this approach has the potential to lead to the diagnosis of substantially more HCV infections compared to the ALT strategy.

There are several limitations to this study. First, NHANES samples include only the U.S. civilian, non-institutionalized population; the exclusion of high-prevalence populations (e.g., incarcerated and homeless persons) likely underestimates anti-HCV prevalence. Second, the sensitivity of the ALT strategy varies with the choice of ULN, which varies by the laboratory conducting the test. In this study, it was found that using a ULN of 31 U/L for men and 20 U/L for women[45] can lead to the identification of nearly 76% of anti-HCV+ people. This would make the ALT strategy comparable to the birth cohort strategy on the basis of sensitivity. However, based on our review of the limitations of risk-based screening and the ALT strategy, we believe that an ALT strategy that recommends gender or other demographic-specific cut-off levels would be no less difficult to implement than the current screening guidelines. Historically, a ULN of 40 U/L has been generally adopted,[10,16,36,43,70] although this may change in the future.[41,45,71]

Third, elevated ALT level was defined based on a one-time measurement of serum ALT activity. It is reasonable to think that if NHANES captured longitudinal data from which persistence of ALT elevation could be examined, the sensitivity of the ALT approach in identifying anti-HCV+ individuals could be diminished,[65] as fewer have PNALT than those

with a single elevated ALT, and consequently the advantage of the birth cohort strategy could be more pronounced.

Finally, key implementation assumptions were made about both strategies, which may not hold in practice and inflate the reported effectiveness of both strategies. The birth cohort strategy assumes that all people born during 1945–1965 would be tested. The ALT strategy implies that providers would have unrestricted access to patient medical records, that ALT levels are regularly evaluated, and all individuals with elevated ALT levels would be tested for HCV infection. Results from this study indicate that substantial proportions of anti-HCV + adults do not have health insurance coverage. Accordingly, not all adults would have access to health care under either strategy. Of those with some access to health services, not all would be tested. For example, under the birth cohort strategy, cohort members may refuse testing because of perceived absence of historic risk factors or fear of stigma. Similarly, under the ALT strategy, ALT levels may not be measured for all patients seeking primary care and a substantial proportion of patients with elevated ALT levels may not be tested for HCV.[9,35]

The CDC and the U.S. Preventive Services Task Force recommend a onetime HCV test for all people born during 1945–1965 without the need for solicitation of behavioral or clinical risk factors.[48,72] The current study provides important evidence for the effectiveness of the birth cohort strategy in identifying HCV cases that would go unidentified using an ALT-only strategy. However, we expect the implementation of the birth cohort screening strategy to happen concurrently with the continued use of ALT-based screening, resulting in averting more HCV-related illnesses and deaths. The results of this study indicate that combining the birth cohort and ALT strategies would identify more than 87% of anti-HCV cases.

The CDC is actively working to support implementation through development of best practices for integrating testing into medical settings (e.g., use of electronic health systems) and development of quality indicators and performance measures. The CDC has augmented testing capacity using Prevention for Public Health Funds and is educating the public about HCV and the need for testing while simultaneously providing clinicians training to improve testing and care through the Know More Hepatitis campaign (cdc.gov/knowmorehepatitis).

The CDC has also conducted panels with stakeholder groups (providers, public health professionals, health plans and payers, laboratories, and federal partners)[48] and is implementing strategies with these partners. The birth cohort HCV testing recommendation has been adopted by the American Medical Association, American College of Physicians, American Association for the Study of Liver Disease, and Infectious Diseases Society of America.[73–75]

It is expected that increasing the proportion of people who have knowledge of their HCV infection will result in increases in linkage to care and treatment as well as provision of prevention services. Among those for whom treatment is contraindicated, prevention strategies to avoid disease transmission (e.g., risk reduction interventions for persons who inject drugs) and attenuate progression of liver disease (e.g., reducing use of alcohol) are available. In conclusion, the CDC recommends that healthcare providers prioritize the

implementation of the birth cohort testing strategy to achieve the public health goals of reducing morbidity and mortality associated with HCV infection.[48]

Acknowledgments

The 50% sensitivity finding for the ALT strategy was previously published in support of the CDC's recommendation to test people born during 1945–1965 for hepatitis C infection.

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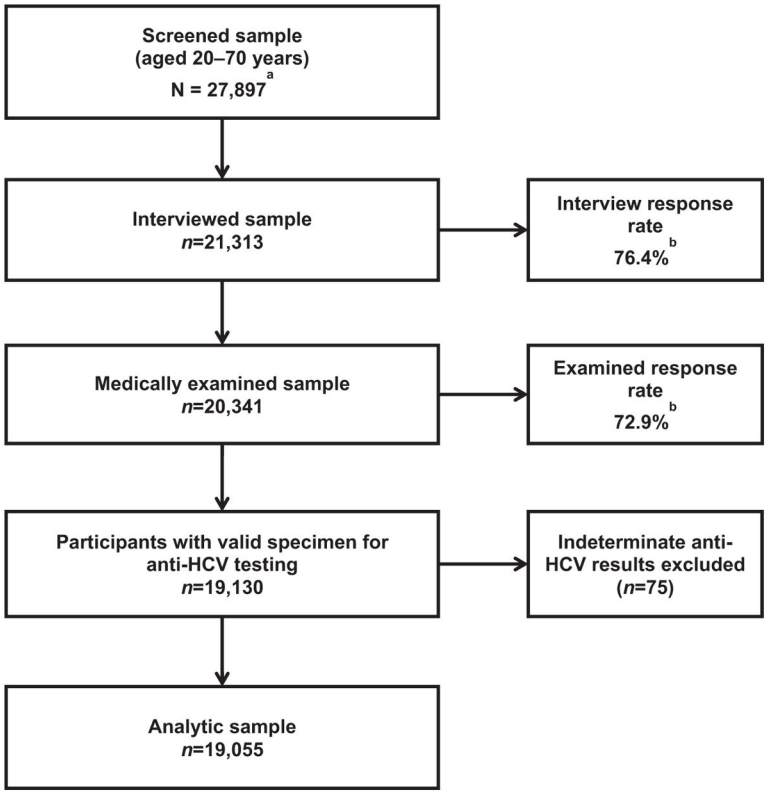

Figure 1.

Participant flow and response rates, adults aged 20–70 years, NHANES 1999–2008

[a]NHANES publishes screen samples for adults aged 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years The screen sample for adults aged 70 years is not published by the single-year age group. Thus, we estimated the screen sample for persons aged 20–70 years based on the interview response rate for persons aged 20–69 years (76.4%; cdc.gov/nchs/nhanes/response_rates_cps.htm).

[b]The denominator used to calculate the response rate was estimated as described above.

HCV, hepatitis C virus; NHANES, National Health and Nutrition Examination Survey

Table 1

Characteristics of adults aged 20–70 years, National Health and Nutrition Examination Survey 1999–2008

	All participants		Anti-HCV-positive	
Characteristic	**Unweighted, *n***	**Weighted, % (95% CI)**	**Unweighted, *n***	**Weighted, % (95% CI)**
Overall	19,055		429	
Age (years; M [SE])	19,055	42.7 (0.2)	429	45.7 (0.5)
Born from 1945 to 1965				
No	11,332	53.2 (52.1, 54.2)	121	23.4 (18.8, 28.9)
Yes	7,723	46.8 (45.8, 47.9)	308	76.6 (71.1, 81.2)
Serum alanine aminotransferase level (U/L)				
<40	16,635	88.2 (87.6, 88.8)	204	50.0 (43.8, 56.2)
≥40	2,264	11.8 (11.2, 12.4)	217	50.0 (43.8, 56.2)
Gender				
Female	9,981	51.0 (50.4, 51.6)	153	37.2 (31.0, 43.7)
Male	9,074	49.0 (48.4, 49.6)	276	62.8 (56.3, 69.0)
Race/ethnicity				
Non-Hispanic white	8,726	70.0 (67.2, 72.7)	178	66.5 (60.9, 71.7)
Non-Hispanic black	3,961	10.9 (9.4, 12.6)	147	20.0 (16.2, 24.5)
Mexican American	4,391	8.3 (7.1, 9.7)	73	6.5 (4.4, 9.5)
Other	1,977	10.8 (9.2, 12.6)	31	7.0 (4.3, 11.1)
Family income to poverty threshold				
>2 times	9,920	67.6 (65.7, 69.4)	138	41.6 (36.1, 47.4)
1–2 times	4,334	19.1 (17.9, 20.4)	128	28.8 (23.6, 34.6)
Below	3,403	13.3 (12.3, 14.3)	137	29.6 (24.4, 35.3)
Health insurance coverage				
Yes	14,179	79.8 (78.5, 81.0)	285	65.3 (59.5, 70.8)
No	4,746	20.2 (19.0, 21.5)	136	34.7 (29.2, 40.5)
Served in the U.S. armed forces				
No	16,977	88.3 (87.6, 89.1)	350	83.2 (77.6, 87.6)

Characteristic	All participants		Anti-HCV-positive	
	Unweighted, *n*	Weighted, % (95% CI)	Unweighted, *n*	Weighted, % (95% CI)
Yes	2,074	11.7 (10.9, 12.4)	78	16.8 (12.4, 22.4)
Average number of alcoholic drinks per day, last year				
0–1	6,168	32.2 (31.0, 33.4)	57	12.7 (9.0, 17.6)
≥2	8,305	46.7 (45.3, 48.1)	223	57.6 (51.4, 63.5)
Unknown	4,582	21.1 (20.0, 22.3)	149	29.7 (25.0, 34.8)
Lifetime drug use (20–59[a] years, *n*=15,138)				
Never	10,963	71.8 (70.3, 73.2)	84	23.2 (18.0, 29.4)
Non-IDU	2,469	17.8 (16.7, 19.0)	93	22.9 (18.8, 27.5)
IDU	297	2.1 (1.8, 2.5)	149	43.4 (37.6, 49.5)
Unknown	1,409	8.3 (7.6, 9.1)	43	10.4 (7.5, 14.4)
Blood transfusion prior to 1992				
No	17,576	93.7 (93.2, 94.1)	354	84.8 (79.9, 88.7)
Yes	1,222	6.3 (5.9, 6.8)	63	15.2 (11.3, 20.1)

[a]NHANES data collection on certain risk factors are limited to participants aged 20–59 years at time of survey.

Anti-HCV, HCV antibody; HCV, hepatitis C virus; IDU, injection drug use; NHANES, National Health and Nutrition Examination Survey

Table 2

Prevalence of hepatitis C virus antibody by participant characteristics, adults aged 20–70 years, National Health and Nutrition Examination Survey 1999–2008

Characteristic	Participants, *n*	Weighted anti-HCV prevalence, % (95% CI)	*p*-value
Overall	19,055	2.0 (1.8, 2.3)	
Born from 1945 to 1965			
No	11,332	0.9 (0.7, 1.1)	ref
Yes	7,723	3.2 (2.8, 3.8)	<**0.001**
Serum alanine aminotransferase level (U/L)			
<40	16,635	1.1 (0.9, 1.3)	ref
≥40	2,264	8.4 (7.0, 9.9)	<**0.001**
Gender			
Female	9,981	1.4 (1.2, 1.8)	ref
Male	9,074	2.5 (2.2, 3.0)	<**0.001**
Race/ethnicity			
Non-Hispanic white	8,726	1.9 (1.6, 2.2)	ref
Non-Hispanic black	3,961	3.6 (3.1, 4.3)	<**0.001**
Mexican American	4,391	1.6 (1.1, 2.2)	0.26
Other	1,977	1.3 (0.8, 2.1)	0.10
Family income to poverty threshold			
>2 times	9,920	1.2 (1.0, 1.5)	ref
1–2 times	4,334	3.0 (2.4, 3.7)	<**0.001**
Below	3,403	4.4 (3.7, 5.3)	<**0.001**
Health insurance coverage			
Yes	14,179	1.6 (1.4, 1.9)	ref
No	4,746	3.4 (2.7, 4.1)	<**0.001**
Served in the U.S. armed forces			
No	16,977	1.9 (1.6, 2.2)	ref
Yes	2,074	2.9 (2.1, 3.9)	<**0.05**
Average number of alcoholic drinks per day, last year			
0–1	6,168	0.8 (0.5, 1.1)	ref
≥2	8,305	2.5 (2.1, 2.9)	<**0.001**
Unknown	4,582	2.8 (2.3, 3.4))	<**0.001**
Lifetime drug use (20–59[d] years, *n*=15,138)			
Never	10,963	0.7 (0.5, 0.9)	ref
Non-IDU	2,469	2.8 (2.2, 3.5)	<**0.001**
IDU	297	44.5 (37.9, 51.3)	<**0.001**
Unknown	1,409	2.7 (1.9, 3.8)	<**0.001**
Blood transfusion prior to 1992			

Characteristic	Participants, *n*	Weighted anti-HCV prevalence, % (95% CI)	*p*-value
No	17,576	1.8 (1.5, 2.1)	ref
Yes	1,222	4.7 (3.4, 6.4)	<**0.001**

Note: Boldface indicates statistical significance.

[a]NHANES data collection on certain risk factors are limited to participants aged 20–59 years at time of survey.

Anti-HCV, HCV antibody; HCV, hepatitis C virus; IDU, injection drug use; NHANES, National Health and Nutrition Examination Survey

Table 3

Hepatitis C virus testing strategy, 1945–1965 birth cohort versus elevated alanine aminotransferase levels

	Testing strategy	
	Elevated ALT	**1945–1965 birth cohort**
Anti-HCV+ adults aged 20–70 years, *n*	3.6	3.6
Adults tested[a], *n*	21.5	85.5
Anti-HCV-positive persons identified by strategy, *n*	1.8	2.8
Current HCV infections identified by strategy[b], *n*	1.4–1.5	2.1–2.4
Sensitivity[c], %	50	76.6

Note: Values are in millions unless otherwise noted.

[a]Based on 10-year average population from 1999–2008 NHANES and may differ from actual total eligible for testing

[b]Based on 75%–85% of weighted frequency of identified anti-HCV-positive persons

[c]Sensitivity was defined as the percentage of total anti-HCV-positive cases identified by the testing strategy.

ALT, alanine aminotransferase; anti-HCV, HCV antibody; HCV, hepatitis C virus; NHANES, National Health and Nutrition Examination Survey